Version with Markings to Show Changes Made

1. (TWICE AMENDED) A rapidly disintegrable solid preparation **[which comprises]** **comprising**

(i) **[a pharmacologically active ingredient that is]** **granules or fine granules of** lansoprazole,

(ii) a sugar and

(iii) a low-substituted hydroxypropylcellulose having 5% **[by weight or more]** to less than 7% by weight of hydroxypropoxyl **[group]** **groups**.

14. (AMENDED) A preparation of Claim **[13]** **1**, wherein **[the pharmacologically active ingredient is comprised in fine granules of the solid preparation]** **said granules or fine granules of lansoprazole are enteric-coated fine granules**.

15. (AMENDED) A preparation of Claim 14, wherein **[(i) a]** **said** sugar and **[(ii) a]** **said** low-substituted hydroxypropylcellulose having 5% **[by weight or more]** to less than 7 % by weight of hydroxypropoxyl **[group]** **groups** are comprised in the solid preparation separately **from** **said enteric-coated** fine granules.

16. (AMENDED) A preparation of Claim 15, wherein **[the]** **said** sugar is in an amount of 5 to 97 parts by weight per 100 parts by weight of the rest of the solid preparation other than **[the]** **said enteric-coated** fine granules.

17. (AMENDED) A preparation of **[the]** Claim 15, wherein the low-substituted hydroxypropylcellulose having 5% **[by weight or more]** to less than 7% by weight of hydroxypropoxyl **[group]** **groups** is in an amount of 3 to 50 parts by weight per 100 parts by weight of the rest of the solid preparation other than **[the]** **said enteric-coated** fine granules.

18. (THRICE AMENDED) A method for preparing a rapidly disintegrable solid preparation comprising

combining a low-substituted hydroxypropylcellulose having 5% **[by weight or more]** to less than 7% by weight of hydroxypropoxyl **[group]** **groups**, **[a pharmacologically active ingredient that is]** **granules or fine granules of** lansoprazole and a sugar.

19. (TWICE AMENDED) A method for improving fast disintegrability of a solid preparation comprising

combining **[a pharmacologically active ingredient that is]** **granules or fine granules of** lansoprazole and a sugar **[which is characterized in that]** **with** a low-substituted hydroxypropylcellulose having 5% **[by weight or more]** to less than 7% by weight of hydroxypropoxyl **[group]** **groups** **[is contained therein]**.

REMARKS

I. Amendments

Claims 1, 18 and 19 have been amended to recite the form of lansoprazole, in accordance with the comparative example in the previously submitted Declaration. The claims have also been modified to conform to U.S. patent practice. These changes introduce no new matter into the specification. No change in inventorship is necessitated by the amendments.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version with Markings to Show Changes Made".

II. Rejection under 35 U.S.C. §103(a)

The rejection of claims 1-7 and 13-19 for obviousness over the Ohno *et al.*, U.S. Patent No. 5,958,453 in view of Shashoua *et al.*, U.S. Patent No. 5,795,909 has been maintained, as the Examiner found the previously submitted Declaration unpersuasive.

Applicants believe that the Examiner misunderstood the previously submitted Declaration. In that Declaration, the procedures for making Example A (representative of a preparation of the present invention) and Example B (representative of Ohno *et al.* formulations) were presented. The Declaration also included comparative testing of Example A to Example B, and concluded that superior results were indeed obtained. To elaborate on the non-obvious nature of the results provided in the previous Declaration, Applicants wish to direct the Examiner's attention to the data for average oral disintegration time found on page 7 of the Declaration. For Example A (representative of a preparation of the present invention), the average oral disintegration time was 29 seconds, while for Example B (representative of Ohno *et al.* formulations), it was nearly double, or 54 seconds. This result is indeed surprising, for it would not have been obvious that the variation in the hydroxypropoxyl group content of L-HPC of the two formulations would have such a dramatic effect on disintegration rate.

Applicants note that the Examiner has concluded that since the Ohno *et al.* reference is interested in dissolution time, the result is not unexpected. Applicants wish to emphasize that they have presented evidence which is not merely indicative of rapid dissolution, but rather demonstrative of an unexpectedly far higher rate of dissolution that would have been anticipated, given the adjustment to the formulation made.

Moreover, the Examiner has commented that the Declaration previously submitted was directed to formulations which were not claimed, mentioning enteric coated granules, granules having a core or mixed powders. Applicants believe that the Examiner may have misunderstood how Comparative Example A was made. The Applicants wish to explain that they made Example A by:

making a granulated powder of a sugar and L-HPC having a hydroxypropyl group content of 5.8% (step (1), found at the bottom of page 4 of the Declaration);

then mixing that granulated powder with enteric coated granules of lansoprazole (step (2), found on page 5 of the Declaration, referring to the method for making the enteric coated granules described on pages 2-4 of the Declaration) to make a mixed powder;

and then tableting the mixed powder (step (3), found on page 5 of the Declaration).

Applicants have amended independent claims 1, 18 and 19 to recite that the lansoprazole is in the form of granules or fine granules, in accordance with the comparative Example A previously provided in the Declaration. The granules fine granules are described on page 16, lines 20-23 and on page 18, line 3 – page 22, line 24. "Fine granules" include "fine granules having a core", and "enteric-coated fine granules" as the Applicants have defined these terms, and also as is understood by those skilled in the art. Therefore, Example A is both representative of, and described by, the claims as amended.

The Declaration provides a comparative Example B, representative of Ohno *et al.* The Examiner has stated that the teaching of Shashoua *et al.* has been cited as teaching lansoprazole as the active ingredient in pharmaceutical formulations, and that when the formulations taught by Ohno *et al.* were combined with the active ingredients of Shashoua *et al.*, the combination rendered the present invention obvious. Applicants aver that they have provided evidence of unexpected results, differentiating their preparation from that of Ohno *et al.* Applicants also aver that the deficiencies of Ohno *et al.* (lack of teaching of the use of a low-substituted hydroxypropylcellulose having 5% to less than 7% by weight of hydroxypropoxyl groups), are not cured by Shashoua *et al.*

Applicants submit that their invention, as set forth in independent claims 1, 18 and 19 as amended, is neither taught nor suggested by the combination of the cited references, as is reinforced by the previously provided Declaration which includes comparative experiments. Claims 2-7 and 13-17 depend upon claim 1, so Applicants submit that these more specific dependent claims are also unobvious.

III. Conclusion

Reconsideration of the claims as amended in view of the arguments made above is solicited. Early allowance of the claims is requested. Should the Examiner believe that a conference with applicants' attorney would advance prosecution of this application, he is respectfully requested to call applicants' attorney.

Respectfully submitted,

Dated: July 24, 2001

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